EDITORIAL

Editorial Comment on “Survival Impact of Total Resected Lymph Nodes in Esophageal Cancer Patients with and without Neoadjuvant Chemoradiation”

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Currently, there is no consensus as to the extent of lymphadenectomy for esophageal squamous cell carcinoma (SCC) post neoadjuvant therapy that would best impact survival. The extent of lymphadenectomy for primary esophagectomy has been addressed by multiple studies. One such study by Peyre and colleagues used an international database of over 2000 patients with either adenocarcinoma or SCC who underwent primary esophagectomy.¹ They found overall survival, and survival by tumor stage, was significantly improved in patients who had sampling of at least 23 lymph nodes. In this study, the presence of nodal metastases was an independent predictor of poor survival. A randomized trial by Omloo and colleagues found that extensive lymphadenectomy did not benefit all patients. This trial found that those with more than eight positive lymph nodes had no survival benefit regardless of the extent of lymph node dissection.²

Nowadays, surgeons rarely see patients who are candidates for primary esophagectomy. Following the results of the CROSS trial in 2012, there has been a dramatic increase in the utilization of neoadjuvant chemotherapy and radiation.³ The CROSS trial demonstrated a strong survival advantage, particularly in squamous cell esophageal carcinoma, for those with local regionally advanced disease who received neoadjuvant therapy compared with primary esophagectomy.³ The median number of resected lymph nodes in the CROSS trial was 15 in the neoadjuvant

therapy group. There was a 31% rate of positive lymph nodes in those who received neoadjuvant therapy compared with 75% in those who underwent primary surgery. The authors did not look further at the impact of the extent of lymphadenectomy on survival.

The current study by Ho and colleagues attempts to clarify the role of lymphadenectomy following esophagectomy for patients with SCC. The study included 3156 patients, 44% of whom received neoadjuvant therapy.⁴ The results confirm that neoadjuvant therapy for patients with SCC results in a relatively high pathologic complete response rate of 29.3%. The average number of resected lymph nodes was 22 and 21 for those who did and did not receive neoadjuvant therapy. Although the survival data in this study shows a significantly worse survival for those patients who received neoadjuvant therapy, those patients had significantly higher initial T and N stage. The number of resected nodes by multivariate analysis was an independent predictor of survival in those who received neoadjuvant therapy. In the author's analysis, the logistic regression model best predicted outcomes with a threshold value of 21 lymph nodes. This finding was not true for those who did not receive neoadjuvant therapy, suggesting that extensive lymphadenectomy may not improve survival for all patients. This is likely due to the fact that 57% of the primary esophagectomy patients were N0 and 30% were N1. Patients with no positive lymph nodes are unlikely to have a survival advantage by taking out more lymph nodes. In contrast, almost 80% of patients who received neoadjuvant therapy had N1 or N2 disease. This indicates that there was a survival advantage to extended lymphadenectomy for those with limited nodal disease. This echoes the findings from previous studies on patients who underwent primary esophagectomy. These results are even more

critical in an era where some patients with SCC are being considered for chemotherapy and radiation without surgery.

The article by Ho et al. adds to the literature on the importance of an adequate lymph node dissection in patients with limited nodal disease, regardless of the use of neoadjuvant therapy. According to the National Cancer Database (NCDB), this is not necessarily the case in practice. Samson and colleagues found that of the 18,777 patients in the NCDB, those who received neoadjuvant therapy were less likely to have 15 or more lymph nodes removed compared with those undergoing primary surgery. In fact, of all variables analyzed, only induction therapy was associated with a decreased likelihood of obtaining 15 or more lymph nodes.⁵ The study looked at patients with both adenocarcinoma and SCC, and the authors concluded that patients undergoing esophagectomy, who had sampling of 15 or more lymph nodes, experienced greater improved median overall survival compared with those who had less than 15 lymph nodes sampled. They also identified a threshold of 25 lymph nodes for improving survival in all patients. Interestingly, Samson and colleagues found a survival advantage with more than 20 lymph nodes resected in those with N0 disease.⁵ They attribute this increase in survival to an increase in staging accuracy. It is unlikely that node-negative patients benefit

from resecting more lymph nodes; however, if at least 20 lymph nodes are sampled, confidence increases in the true node-negative status.⁵ The optimal number of resected lymph nodes at the time of esophagectomy, regardless of the use of neoadjuvant therapy, should be greater than 15 and potentially greater than 20.

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